

## REMARKS/ARGUMENTS

No claims are being cancelled. Claims 7 and 11 are being amended. No new matter has been introduced by the amendments.

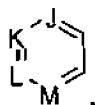
After entry of the above amendments, claims 1-114 will be pending.

### Election/Restriction

In the Office Action, the Examiner acknowledges Applicants' election of a single species, indicates that the elected species is free of prior art, and states that the initial search was extended. The Examiner further indicates that the claims were examined "only to the extent that they read on the elected invention."

The present claims are drawn to a single invention and restriction, to the extent that it is applicable at all, should be based only on a restriction as to species (as reflected in the Restriction Requirement previously issued in this case). In this regard, claim 1 is a genus claim (*i.e.*, generic) that links the species of claims 2-114. MPEP 809.03. Genus claims that link together species claims act to prevent restriction between inventions, even when the inventions would otherwise be divisible. MPEP 809.03.

Here, each of claims 2-114 contains all of the limitations of claim 1. Specifically, claim 1 relates to compounds of Formula XIX wherein R<sub>3</sub> and R<sub>4</sub> are taken together to form a substituted or unsubstituted 5- or 6-membered ring. All of the remaining independent claims specify particular arrangements of the ring formed by R<sub>3</sub> and R<sub>4</sub>. For example, independent claim 42 specifies that the ring formed by R<sub>3</sub> and R<sub>4</sub> is



and independent claim 65 specifies that the ring formed by R<sub>3</sub> and R<sub>4</sub> is

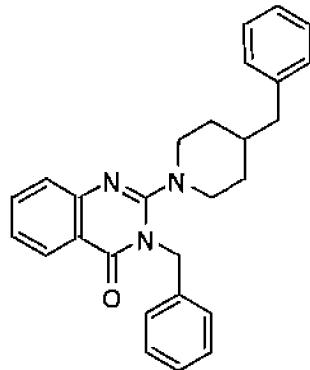


Similar analyses apply to each of the pending independent claims.

Accordingly, claim 1 is a linking claim that should be examined with the invention elected, and if allowable, the restriction requirement should be withdrawn. MPEP 809.

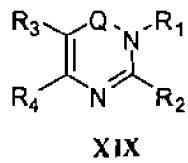
### Rejections Under 35 USC §102

Claims 1-7, 16-19, 22, 23, 25-27, 30-33, 41-43, 87, 88, 99 and 103 are rejected as being anticipated by the 3-(phenylmethyl)-2-[4-(phenylmethyl)-1-piperidinyl]-4(3H)-quinazolinone anthranilic acid disclosed in Kesarwani *et al.*.



3-(Phenylmethyl)-2-[4-(phenylmethyl)-1-piperidinyl]-4(3H)-quinazolinone

In contrast to Kesarwani *et al.*, the present invention relates to compounds having the formula:



wherein  $R_2$  is -UV, where  $U$  is a moiety providing 1-6 atom separation between  $V$  and the ring to which  $R_2$  is attached and  $V$  comprises a basic nitrogen atom that is capable of interacting with a carboxylic acid side chain of an active site residue of a protein (*emphasis added*).

Because  $U$  requires at least one atom, the ring nitrogen atom of the piperidinyl substituent of Kesarwani *et al.* necessarily must be read as being part of  $U$ . Even if the remainder of the piperidinyl substituent is read to be part of  $V$ , it clearly does *not* possess the basic nitrogen atom required of  $V$ . Accordingly, the 3-(phenylmethyl)-2-[4-(phenylmethyl)-1-piperidinyl]-4(3H)-

quinazolinone anthranilic acid of Kesarwani *et al.* does not encompass all of the features of the present claims and the rejection under 35 USC §102 should be withdrawn.

### Rejections Under 35 USC §112, Second Paragraph

Claims 1-10, 15-33, 36, 42, 43, 55-61, 87, 88, 95, 99, 100 and 103 are rejected as allegedly being indefinite.

With respect to the term “substituted,” the Examiner appears to suggest that the claims are indefinite because the claims do not articulate the particular moieties which facilitate substitution. However, the claim need not list every possible substituent for one of ordinary skill in the art to know what is within the scope of the claim. See *Ex parte* Lani S. Kangas, Mieczyslaw H. Mazurek, Kurt C. Melancom, Walter R. Romanko, and Audrey A. Sherman, Appeal No. 2002-0250 (BPAI 2002) (copy attached). The claim may be broad in terms of possible R groups, but that alone does not make the claim indefinite. MPEP 2173.04.

In addition, the specification provides guidance in the interpretation of the term “substituted”. Specifically, the specification at paragraph [0098] states:

In general, a non-hydrogen substituent may be any substituent that may be bound to an atom of the given moiety that is specified to be substituted. Examples of substituents include, but are not limited to, aldehyde, alicyclic, aliphatic, alkyl, alkylene, alkylidene, amide, amino, aminoalkyl, aromatic, aryl, bicycloalkyl, bicycloaryl, carbamoyl, carbocyclyl, carboxyl, carbonyl group, cycloalkyl, cycloalkylene, ester, halo, heterobicycloalkyl, heterocycloalkylene, heteroaryl, heterobicycloaryl, heterocycloalkyl, oxo, hydroxy, iminoketone, ketone, nitro, oxaalkyl, and oxoalkyl moieties, each of which may optionally also be substituted or unsubstituted.

Definitions for the term “substituent” can also be found in the literature. For example, Hawley’s Condensed Chemical Dictionary 1056 (13<sup>th</sup> Ed. 1997) defines “substituent” as “[a]n atom or radical that replaces another in a molecule as the result of a reaction” (see attached).

Accordingly, one of ordinary skill in the art would understand the bounds of the term “substituted” as it is used in the present claims. Therefore, the rejection is improper and should be withdrawn.

In addition, certain claims are rejected because the phrase “U is a moiety providing 1-6 atom separation” is allegedly indefinite. However, those skilled in the art would readily

understand that U is a “linker” that joins V to the ring carbon of the compound of Formula XIX. As such, the atoms in the direct chain of atoms that link V to the ring are the atoms that provide the separation between V and the ring. Furthermore, Applicants provide ample descriptions of what may be used as V. *See, e.g.*, Specification at paragraphs [0235]-[0244]. In light of the foregoing, the rejection is improper and should be withdrawn.

The Examiner also indicates that use of the transitional phrase “comprising” in the claims is indefinite. The rejection is apparently based on the assertion that the term “comprising” is open-ended. Applicants acknowledge that the term “comprising” is open-ended. However, Applicants are not aware of any provisions in the patent laws that renders the term “comprising” indefinite when used as a transitional phrase in a claim. In fact, the MPEP and patent case law recognize that “‘comprising’ is a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim.” *MPEP* §2111.03; *Genentech, Inc. v. Chiron Corp.*, 112 F.3d 495, 501, 42 USPQ2d 1608, 1613 (Fed. Cir. 1997). If the Examiner is relying on any particular provisions that render claims with the transitional phrase “comprising” *per se* indefinite, Applicants request that the Examiner bring such information to Applicants’ attention. In the absence of such information, the rejection of the claims is inappropriate and should be withdrawn.

The claims are also rejected because the phrase “V comprises a basic nitrogen atom that is capable of interacting with a carboxylic acid side chain of an active site residue of a protein” is allegedly indefinite. In making the rejection, the Examiner suggests that it is unclear whether the ring nitrogen [of claim 7] is capable of interacting with the carboxylic acid. However, those skilled in the art would readily appreciate that the ring nitrogen atoms of the moieties of claim 7 (including the piperadine) do *not* constitute the basic nitrogen atom required by the claims. As discussed above, because U requires at least one atom, the ring nitrogen atom of the moieties of claim 7 necessarily must be read as being part of U. Accordingly, the ring nitrogen atom of the moieties cannot constitute the basic nitrogen atom required of V. The fact that the aforementioned ring nitrogens do not provide the necessary basic nitrogen is precisely why moieties of the type specified in claim 11 can be used in connection with the present invention, even though those moieties do not even contain a ring nitrogen. To clarify this point, claims 7 and 11 are being amended to require that at least one substituent R<sub>8</sub> is present and that said at

least one R<sub>8</sub> provides the basic nitrogen atom of V. Accordingly, the rejection should be withdrawn.

Claim 1 is also rejected because use of the phrase “R<sub>3</sub> and R<sub>4</sub> are taken together to form... a 5 or 6 membered ring” is indefinite. However, use of the term “ring” in reference to chemical species is commonplace and definitions of the term “ring” in this context is replete in the literature. For example, Hawley’s Condensed Chemical Dictionary 972 (13<sup>th</sup> Ed. 1997) defines ring compounds to include cyclic, alicyclic, aromatic and heterocyclic compounds (see attached). Hawley’s Condensed Chemical Dictionary 32, 92, 322, 569 (13<sup>th</sup> Ed. 1997) then goes on to individually define the terms “alicyclic”, “aromatic”, “cyclic compounds” and “heterocyclic” (see attached). Accordingly, one of ordinary skill in the art would understand the bounds of the phrase “R<sub>3</sub> and R<sub>4</sub> are taken together to form... a 5 or 6 membered ring” as it is used in the present claims. Therefore, the rejection is improper and should be withdrawn.

### **Double Patenting**

The Examiner has provisionally rejected claims 1-10, 15-33, 36, 42, 43, 55-61, 87, 88, 95, 99, 100 and 103 under the doctrine of non-statutory obviousness-type double patenting as being unpatentable over claims 1-5, 8, 9, 11-17, 19, 23, 26, 27, 29, 37-39, 51-57, 83, 84, 95, 99 and 111 of copending Application No. 10/809,635. Since the rejection is provisional, Applicants intend to address the rejection when one or both of the applications are otherwise in condition for allowance.

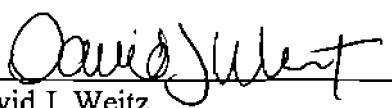
**CONCLUSION**

Applicants earnestly believe that they are entitled to a letters patent, and respectfully solicit the Examiner to expedite prosecution of this patent application to issuance. Should the Examiner have any questions, the Examiner is encouraged to telephone the undersigned.

Respectfully submitted,

Dated: July 27, 2006

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*Hawley's*

*Condensed Chemical*

*Dictionary*

*THIRTEENTH EDITION*

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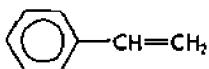
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**Grade:** Technical 99.2%, polymer 99.6%.

**Hazard:** Flammable, moderate fire risk, explosive limits in air 1.1-6.1%, must be inhibited during storage. Toxic by ingestion and inhalation. TLV: 50 ppm in air.

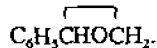
**Use:** Polystyrene; SBR, ABS, and SAN resins; protective coatings (styrene-butadiene latex, alkyds); styrenated polyesters; rubber-modified polystyrene; copolymer resins; intermediate.



**styrene nitrosite.** A compound resulting from the reaction between styrene and nitrogen dioxide and used as a qualitative or quantitative specific test for monomeric styrene in mixtures with other hydrocarbons.

**styrene oxide.**

CAS: 96-09-3.



**Properties:** Colorless to pale-straw-colored liquid. Boiling range 194.2-195°C (5-95%), fp -36.6°C, flash p 180°F (82.2°C) (COC), refr index 1.5328 (25°C), d 1.0469 (25/4°C). Miscible with benzene, acetone, ether, and methanol. Combustible.

**Hazard:** Toxic by ingestion and inhalation. Use: Highly reactive organic intermediate.

**"Styresol"** [Reichhold]. TM for a group of styrenated alkyd resins with air-drying and baking properties and high resistance to gasoline, alkalies, acids, and water.

**"Styrofoam"** [Dow]. TM for expanded cellular polystyrene (available in colors).

**Use:** Insulating materials; light-weight materials for boats, toys, etc.; separators in packing containers; airport runways; highway construction; battery cases.

**"Styron"** [Dow]. TM for polystyrene resins, general purpose, medium and high impact, heat and impact-heat resistant, and light-stabilized resins ("Styron Vcrelite"). Available in wide range of translucent and opaque colors, as well as natural and crystal.

**Use:** Packaging, toys, appliance parts, bottle closures and containers, hot and cold drinking cups, television cabinet backs, automotive components and machine housings, lighting equipment.

**styryl carbinol.** See cinnamic alcohol.

**suberane.** See cycloheptane.

**suberic acid.** (octanedioic acid).



**Properties:** Colorless crystals from water. Mp 143°C, bp 279°C (100 mm Hg). Partially soluble in water and ether; soluble in alcohol. Combustible.

**Derivation:** Oxidation of oleic acid with nitric acid. **Use:** Intermediate for the synthesis of drugs, dyes, and high polymers.

**suberone.** See cycloheptanone.

**"Sublaprints"** [Holliday]. TM for uncut disperse dyestuffs.

**Use:** In transfer printing applications.

**sublimation.** The direct passage of a substance from solid to vapor without appearing in the intermediate (liquid) state. An example is solid carbon dioxide which vaporizes at room temperature; the conversion may also be from vapor to solid under appropriate conditions of temperature.

**subnuclear particle.** A particle either found in the nucleus or observed coming from the nucleus as the result of nuclear reaction or rearrangement, i.e., neutrons, mesons, etc.

**substance.** Any chemical element or compound. All substances are characterized by a unique and identical constitution and are thus homogeneous. "A material of which every part is like every other part is said to be homogeneous and is called a substance." (Black and Conant, *Practical Chemistry*.) See homogeneous.

**substantive dye.** See direct dye.

**substituent.** An atom or radical that replaces another in a molecule as the result of a reaction. See substitution.

**substitute natural gas.** See synthetic natural gas.

**substitution.** The replacement of one element or radical by another as a result of a chemical reaction. Chlorination of benzene to produce chlorobenzene is a typical example; in this case a chlorine atom replaces a hydrogen atom in the benzene molecule.

**substrate.** (1) A substance upon which an enzyme or ferment acts. (2) Any solid surface on which a coating or layer of a different material is deposited.

**subtilin.** An antibiotic produced by the metabolic processes of strain of *Bacillus subtilis*. It is a cyclic polypeptide similar to bacitracin in chemical structure and antibiotic activity, but not as important clinically. Subtilin is active against many Gram-positive bacteria, some Gram-negative cocci, and some species of fungi. It is a surface tension

**Properties:** White, crystalline alkaloid. Slightly soluble in water, chloroform, and ether. Mp 201.5°C, sublimes 170–180°C (20 mm Hg).

**Derivation:** From castor oil seeds and leaves.

**Hazard:** Toxic by ingestion.

**Use:** Biochemical research.

**ricinoleic acid.** (*cis*-12-hydroxyoctadec-9-enoic acid; 12-hydroxyoleic acid; castor oil acid).

**CAS:** 141-22-0.

$\text{CH}_3(\text{CH}_2)_5\text{CH}(\text{OH})\text{CH}_2\text{CH}:\text{CH}(\text{CH}_2)\text{COOH}$ . A C<sub>18</sub> unsaturated fatty acid that comprises 80% of the fatty acid content of castor oil.

**Properties:** Colorless to yellow, viscous liquid. D 0.940 (27.4/4C), mp 5.5°C, bp 226°C (10 mm Hg), ref index 1.4697 (20C), dextrorotatory. Soluble in most organic solvents; insoluble in water. Combustible.

**Derivation:** Saponification of castor oil.

**Use:** Soaps, Turkey red oil, textile finishing, source of sebacic acid and heptanol, ricinoleate salts, 12-hydroxystearic acid.

**ricinoleyl alcohol.** (9-octadecen-1,12-diol).

$\text{CH}_3(\text{CH}_2)_5\text{CH}(\text{OH})\text{CH}_2\text{CH}:\text{CH}(\text{CH}_2)\text{CH}_2\text{OH}$ . The fatty alcohol derived from ricinoleic acid. It has a long, straight chain with one double bond and one hydroxyl group in a secondary position besides the primary group on the end. Available as a 90% product.

**Properties:** Colorless, nondrying liquid at room temperature. Iodine value 91.8%, cloud point -12.2°C, boiling range 170–328°C, viscosity 51 (SSU/21C). Combustible.

**Derivation:** Reduction of acid made from castor oil.

**Impurities:** Oleyl and linoleyl alcohols.

**Use:** Protective coatings, polyesters, plasticizers, organic synthesis, pharmaceuticals, lubricants, surface-active agents.

**ricinus oil.** See castor oil.

**Rieglers test.** A test for nitrous acid using sodium naphthionate and  $\beta$ -naphthol.

**Riehm quinoline synthesis.** Formation of quinoline derivatives by prolonged heating of arylamine hydrochlorides with ketones with or without use of aluminum chloride or phosphorus pentachloride.

**Riemschneider thiocarbamate synthesis.**

The action of concentrated sulfuric acid followed by treatment with ice water serves to transform arylthiocyanates into the corresponding thiocarbamates.

**Riley oxidations.** Oxidations of organic compounds with selenium dioxide, e.g., the oxidation of active methylene groups to carbonyl groups.

**"Rilsan."** TM for nylon 11.

See nylon.

**RIM.** Abbreviation for reaction injection molding.

**ring compound.** See cyclic compound; alicyclic; aromatic; heterocyclic.

**Ringer's solution.** Physiologic solution containing 0.650 g sodium chloride, 0.014 g potassium chloride, 0.0129 g calcium chloride, 0.020 g sodium bicarbonate, 0.001 g monosodium phosphate, 0.200 g dextrose in 100 g water. It is isotonic with frog blood serum.

**ring whizzer.** A fluxional molecule frequently encountered in organometallic chemistry in which rapid rearrangements occur by migrations about unsaturated organic rings.

**ripening.** (cheese). See aging; curing.

**ristocetin.** An antibiotic produced by the fermentation of *Nocardia lurida*, a species of Actinomycetes. The antibiotic has two components, ristocetin A and ristocetin B. The commercial product is a lyophilized preparation representing a mixture of A and B, of which B is no more than 25%.

**Properties:** White or tan crystals or powder; practically odorless. Freely soluble in water; practically insoluble in organic solvents.

**Grade:** USP.

**Use:** Medicine.

**Ritter reaction.** Formation of amides by addition of olefins or secondary and tertiary alcohols to nitriles in strongly acidic media.

**Rittinger's law.** The energy required for reduction in particle size of a solid is directly proportional to the increase in surface area.

See Kick's law.

**Rn.** Symbol for radon.

**RNA.** Abbreviation for ribonucleic acid.

**RNA polymerase.** An enzyme essential in imparting the DNA genetic code to ribonucleic acid (RNA).

**roasting.** Heating in the presence of air or oxygen.

Most commonly used in converting natural metal sulfide ores to oxides as a first step in recovery of metals such as zinc, lead, copper, etc. Roasting is an oxidation process.

See smelting.

**Robinson annellation reaction.** Formation of six-membered-ring  $\alpha,\beta$ -unsaturated ketones by condensation of cyclohexanones with methyl vinyl ketone or its equivalents, followed by an intramolecular aldol condensation.

**Robinson-Schöpf reaction.** Synthesis of tropinones from a dialdehyde, methylamine, and acetonedicarboxylic acid.

and used as food supplements (see carrageenan, agar), soil conditioners, animal feeds, and a source of iodine; they also contain numerous minerals, vitamins, proteins, lipids, and essential amino acids. Alginic acid is another important derivative. Blue-green algae are water contaminants and are toxic to fish and other aquatic life. Phosphorus compounds in detergent wastes stimulate the growth of algae to such an extent that overpopulation at the water surface prevents light from reaching many of the plants; these decompose, removing oxygen and releasing carbon dioxide, thus making the water unsuitable for fish. Algae are being used in treatment of sewage and plant effluent in a proprietary flocculation process.

See eutrophication; agar; biomass.

**Algar-Flynn-Oyamada reaction.** Alkaline hydrogen peroxide oxidation of *o*-hydroxyphenyl styryl ketones (chalcones) to flavonols via the intermediate dihydroflavonols.

**algicide.** Chemical agent added to water to destroy algae. Copper sulfate is commonly employed for large water systems.

**algin.** A hydrophilic polysaccharide (phycocolloid or hydrocolloid) found exclusively in the brown algae. It is analogous to agar. The seaweed (giant kelp) is sea harvested, water extracted, and refined. U.S. (California) and Great Britain are the chief producers.

See alginic acid; alginate.

**alginate.** Any of several derivatives of alginic acid (e.g., calcium, sodium, or potassium salts or propylene glycol alginate). They are hydrophilic colloids (hydrocolloids) obtained from seaweed. Sodium alginate is water soluble but reacts with calcium salts to form insoluble calcium alginate. Use: Food additive (thickener, stabilizer), yarns and fibers, medicine (first-aid dressings), meat substitute, high-protein food analogs.

**alginic acid.**  $(C_6H_8O_6)_n$ .

A polysaccharide composed of  $\beta$ -D-mannuronic acid residues linked so that the carboxyl group of each unit is free, while the aldehyde group is shielded by a glycosidic linkage. It is a linear polymer of the mannuronic acid in the pyranose ring form.

Properties: White to yellow powder possessing marked hydrophilic colloidal properties for suspending, thickening, emulsifying, and stabilizing. Insoluble in organic solvents, slowly soluble in alkaline solutions. Absorbs up to 300 times its weight of water.

Grade: Refined (food), technical (commercial), NF (sodium alginate), FCC.

Use: Food industry as thickener and emulsifier; protective colloid in ice cream, toothpaste, cosmetics, pharmaceuticals, textile sizing, paper coatings; waterproofing agent for concrete; boiler water treat-

ment; oil-well drilling muds; storage of gasoline as a solid.

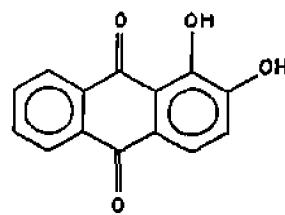
**alicyclic.** A group of organic compounds characterized by arrangement of the carbon atoms in closed ring structures sometimes resembling boats, chairs, or even birdcages. These compounds have properties resembling those of aliphatics and should not be confused with aromatic compounds having the hexagonal benzene ring. Alicyclics comprise three subgroups: (1) cycloparaffins (saturated); (2) cycloolefins (unsaturated, with two or more double bonds); and (3) cycloacetylenes (cyclenes) with a triple bond. The best-known cycloparaffins (sometimes called naphthenes) are cyclopropane, cyclohexane, and cyclopentane; typical of the cycloolefins are cyclopentadiene and cyclooctatetraene. Most alicyclics are derived from petroleum or coal tar. Many can be synthesized by various methods.

**aliphatic.** One of the major groups of organic compounds, characterized by straight- or branched-chain arrangement of the constituent carbon atoms. Aliphatic hydrocarbons comprise three subgroups: (1) paraffins (alkanes), all of which are saturated and comparatively unreactive, the branched-chain types being much more suitable for gasoline than the straight-chain; (2) olefins (alkenes or alkadienes), which are unsaturated and quite reactive; (3) acetylenes (alkynes), which contain a triple bond and are highly reactive. In complex structures, the chains may be branched or cross-linked. See alicyclic; aromatic; chain.

**aliquot.** A part that is a definite fraction of a whole, as in aliquot samples for testing or analysis.

**alizarin.** (1,2-dihydroxyanthraquinone; C.I. 58000).  $C_9H_4(CO)_2C_6H_2(OH)_2$ .

Parent form of many dyes and pigments including mordants.



Properties: Orange-red crystals; brownish-yellow powder. Mp 289°C, bp 430°C (sublimable). Soluble in aromatic solvents, hot methanol, and ether; sparingly soluble in water; moderately soluble in ethanol. Combustible.

Derivation: Anthracene is oxidized to anthraquinone, the sulfonic acid of which is then fused with caustic soda and potassium chloride; the melt is run into hot water and the alizarin precipitated with hydrochloric acid. Occurs naturally in madder root.

**Use:** Sequestering agent for iron, calcium, and magnesium ions; soap builder; detergent mixtures; deflocculator in drilling muds, paper, ceramics and textiles.

**Armstrong's acid.** (naphthalene-1,5-disulfonic acid).  $C_{10}H_4(SO_3H)_2$ .

**Properties:** White, crystalline solid. Soluble in water.

**Derivation:** Sulfonation of naphthalene with fuming sulfuric acid at low temperature followed by separation from the 1,6-isomer.

**Use:** Dye intermediate.

**Arndt-Eistert synthesis.** Procedure for converting an acid to its next higher homolog.

**"Arnel"** [Hoechst Celanese]. TM for an acetate fiber made from cellulose triacetate. It has a higher melting point, and is less soluble than cellulose acetate.

See acetate fiber; cellulose triacetate.

**aromatic.** (arene). A major group of unsaturated cyclic hydrocarbons containing one or more rings, typified by benzene, which has a 6-carbon ring containing three double bonds. The vast number of compounds of this important group, derived chiefly from petroleum and coal tar, are rather highly reactive and chemically versatile. The name is due to the strong and not unpleasant odor characteristic of most substances of this nature. Certain 5-membered cyclic compounds such as the furan group (heterocyclic) are analogous to aromatic compounds.

**Note:** The term "aromatic" is often used in the perfume and fragrance industries to describe essential oils that are not aromatic in the chemical sense.

**aromaticity.** A stable electron shell configuration in organic molecules, especially those related to benzene.

See resonance; orbital theory.

**aromatization.** See hydroforming.

**"Arosurf TA100"** [Witco]. (distearyl dimethylammonium chloride).

**CAS:** 107-64-2. TM for powder cationic-quaternary fabric softener.

**Use:** For retail powdered detergent-softener, industrial laundry and paper-softening formulas, and cosmetic formulations.

**arrack.** An oriental distilled liquor which is obtained from palm or rice juice.

**arrest point.** The temperature at which a system of more than one component, being heated or cooled, absorbs or yields heat without changing temperature.

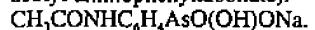
**Arrhenius, Svante.** (1859-1927). A native of Sweden, he won the Nobel prize in chemistry in 1903. He is best known for his fundamental investigations on electrolytic dissociation of compounds in water and other solvents, and for his basic equation stating the increase in the rate of a chemical reaction with rise in temperature:

$$\frac{d \ln k}{dT} = \frac{A}{RT^2}$$

in which  $k$  is the specific reaction velocity,  $T$  is the absolute temperature,  $A$  is a constant usually referred to as the energy of activation of the reaction, and  $R$  is the gas-law constant.

**arrowroot.** (maranta). The starch that is obtained from the roots of the maranta plant, which has many uses, including food ingredients, cosmetics, glues, and starches.

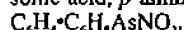
**arsacetin.** (sodium acetylarsanilate; sodium *p*-acetyl aminophenylarsonate).



**Properties:** White, crystalline powder; odorless; tasteless. Free of arsenous or arsenic acid. Solutions will admit of thorough sterilization. Soluble in cold water, but more so in warm water.

**Use:** Medicine (antisyphilitic).

**arsanilic acid.** (atoxylic acid; *p*-aminobenzene-*p*-soronic acid; *p*-aminophenylarsonic acid).



**Properties:** White, crystalline powder; practically odorless. Mp 232C. Soluble in hot water; slightly soluble in cold water, alcohol, and acetic acid; insoluble in acetone, benzene, chloroform, and ether.

**Derivation:** By condensing aniline with arsenic acid, removing the excess of aniline by steam distillation in alkaline solution, and setting the acid free using hydrochloric acid.

**Hazard:** A poison. Yields flammable vapors on heating above melting point.

**Use:** Arsanilates, manufacture of arsenical medicinal compounds such as arsphenamine, veterinary medicine, grasshopper bait.

**arsenic.**

**CAS:** 7440-38-2. As. A nonmetallic element of atomic number 33, group Va of periodic table, aw 74.9216; valences of 2, 3, 5; no stable isotopes.

**Properties:** Silver-gray, brittle, crystalline solid that darkens in moist air. Allotropic forms: black, amorphous solid ( $\beta$ -arsenic); yellow, crystalline solid, d 5.72 (commercial product ranges from 5.6 to 5.9), mp 814C (36 atm), sublimes at 613C (1 atm), Mohs hardness 3.5. Insoluble in water and in caustic and nonoxidizing acids. Attacked by hydrochloric acid in presence of oxidant. Reacts with nitric acid. Low thermal conductivity; a semiconductor.

**Derivation:** Flue dust of copper and lead smelters from which it is obtained as white arsenic (arsenic

**Properties:** Viscous, brown liquid. Soluble in petroleum solvents and other common organic solvents. Formulated principally as liquid for spray applications corresponding to natural pyrethrins. **Hazard:** Toxic by inhalation and ingestion. **Use:** Insecticide with applications similar to allethrin and other analogs. See furethrin; barthrin; ethythrin.

**cyclic compound.** An organic compound whose structure is characterized by one or more closed rings; it may be mono-, bi-, tri-, or polycyclic depending on the number of rings present. There are three major groups of cyclic compounds: (1) alicyclic, (2) aromatic (also called arene), and (3) heterocyclic. For more detailed information, consult specific entries.

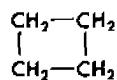
**cyclizine hydrochloride.** (1-diphenylmethyl-4-methylpiperazine hydrochloride). CAS: 303-25-3.  $(C_6H_5)_2CHC_6H_4N_2CH_3 \cdot HCl$ . **Properties:** White, crystalline powder or small colorless crystals; odorless or nearly so; bitter taste. Mp 285°C (decomposes). Slightly soluble in water, alcohol, chloroform; insoluble in ether; pH (2% solution) 4.5–5.5. **Grade:** USP. **Use:** Medicine (antiemetic).

**cycloaliphatic epoxy resin.** (cycloalkenyl epoxides). A polymer prepared by epoxidation of multicycloalkenyls (polycyclic aliphatic compounds containing carbon-carbon double bonds) with organic peracids such as peracetic acid. Resistant to high temperatures.

**Use:** Space vehicles, outdoor electrical installations in polluted and humid atmospheres, high-temperature adhesives.

**cyclobarbital.** [5-(1-cyclohexenyl)-5-ethylbarbituric acid; tetrahydrophenobarbital]. CAS: 52-31-3.  $C_{12}H_{16}N_2O_4$ . **Properties:** White crystals or crystalline powder; odorless; bitter taste. Mp 170–174°C. Soluble in alcohol or ether; very slightly soluble in cold water or benzene. **Derivation:** Hydrogenation of phenobarbital with colloidal palladium in alcohol as a catalyst. **Hazard:** See barbiturates. **Use:** Medicine (hypnotic, sedative).

**cyclobutane.** (tetramethylene). CAS: 287-23-0.  $C_4H_8$ .



**Properties:** Colorless gas. D 0.7083 (11°C), bp 13°C, fp –80°C, flash p <50°F. Insoluble in water; soluble in alcohol and acetone.

**Derivation:** Catalytic hydrogenation of cyclobutene. **Hazard:** Flammable, dangerous fire risk.

**cyclobutene.** (cyclobutylene).  $C_4H_6$ .

**Properties:** Gas. D 0.733, bp 2.0°C.

**Derivation:** From petroleum.

**Hazard:** Flammable, dangerous fire risk.

**cyclocitrylideneacetone.** See ionone.

**cyclocumarol.**  $C_{20}H_{16}O_4$ .

A synthetic blood anticoagulant.

**Properties:** White, crystalline powder; slight odor. Mp 164–168°C. Soluble in water; slightly soluble in alcohol.

**cycloheptane.** (heptamethylene; suberane).

CAS: 291-64-5.  $C_7H_{14}$ .

**Properties:** Colorless liquid. D 0.809, bp 117, fp –12°C, aniline equivalent –6, flash p >70°F (20°C). Soluble in alcohol; insoluble in water.

**Grade:** Technical.

**Hazard:** Flammable, dangerous fire risk. Narcotic by inhalation.

**Use:** Organic synthesis.

**cycloheptanone.** (suberone).

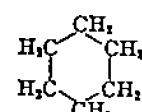
CAS: 502-42-1.  $C_7H_{12}O$ .

**Properties:** Colorless liquid; peppermint odor. Bp 179°C, d 0.95. Insoluble in water; soluble in ether and alcohol. Combustible.

**Use:** Research, intermediate.

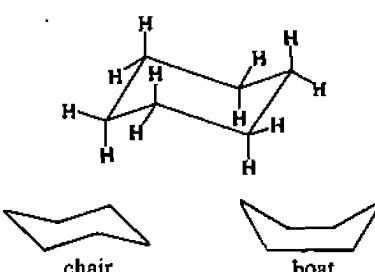
**cyclohexane.** (hexamethylene; hexanaphthene; hexahydrobenzene).

CAS: 110-82-7.  $C_6H_{12}$ ; 47th highest-volume chemical produced in U.S. (1995).



**Structure:** A typical alicyclic hydrocarbon. It exists in two modifications called the "boat" and the "chair," as shown. This is due to slight distortion of the bond angles in accordance with the modified version of Baeyer's strain theory. Cyclohexane has been studied extensively on a theoretical basis in a branch of advanced chemistry called conformational analysis.

See conformation.



707 High molecular weight polyol ester.  
 707A High molecular weight polyol ester.  
 Use: High-temperature vinyl electrical insulation.  
 900 High molecular weight polyester.  
 Use: Plasticizer for polyvinyl acetate.

**"Hercolube" [Aqualon].** TM for synthetic lubricant base stocks. Saturated aliphatic ester of pentaerythritol for plasticizing vinylidene chloride. Derived from pentaerythritol esters of saturated fatty acids.

**"Hercolyn" D [Aqualon].** TM for a pale, viscous liquid; the hydrogenated methyl ester of rosin.  
 Use: Plasticizing resin.

**hercules trap.** Water-measuring liquid trap used in aquametry when the material collected is heavier than water.

**"Herculoid" [Aqualon].** TM for nitrocellulose containing 10.9–11.2% nitrogen.  
**Hazard:** See nitrocellulose.  
 Use: Pyroxylin plastics.

**"Herculon" [Aqualon].** TM for polypropylene olefin fibers. Available in bulked continuous and continuous multifilament yarns, staple, and uncut tow.  
 Use: Apparel, home furnishings, and industrial applications.

**heroin.** See diacetylmorphine.

**herring oil.** See fish oil.

**Herschbach, Dudley R.** (1932– ). Awarded the Nobel prize in chemistry in 1986 for work reporting that the energies of reactions of crossed molecular beams of isolated alkali metal atoms and alkyl halide molecules appeared mostly as vibrational excited states of products. This method of studying all types of chemical reactions led to a more detailed knowledge of reaction processes. Doctorate awarded from Harvard in 1958.

**Herzberg, Gerhard.** (1904– ). A German-born physicist who won the Nobel prize for chemistry in 1971 for his work on the composition of molecules. His research involved the spectroscopy of atoms and molecules and their excitation behavior. He became a Canadian citizen and was the director of the Division of Pure Physics of the National Research Council of Canada.

**Herzig-Meyer determination of *N*-alkyl groups.** *N*-alkylamines are refluxed with hydroiodic acid and the quaternary alkyl ammonium iodides are pyrolyzed to split off alkyl iodide, which is determined gravimetrically by conversion to silver iodide or titrated as iodate.

**Herz reaction; Herz compounds.** Formation of *o*-aminothiophenols by heating aromatic amines with excess sulfur monochloride. The first products formed are thiazothionium halides known as Herz compounds. If the position next to the amino group is unoccupied, chloride is substituted at this position during the reaction.

**hesperidin.**

CAS: 520-26-3.  $C_{28}H_{34}O_{15}$ . A natural bioflavonoid of the flavanone group.

**Properties:** Fine needles. Mp 258–262°C. Soluble in dilute alkalies and pyridine.

**Derivation:** Extraction from citrus fruit peel.

**Use:** Synthetic sweetener research.

**Hess's law.** The heat evolved or absorbed in a chemical process is the same whether the process takes place in one or in several steps; also known as the law of constant heat summation.

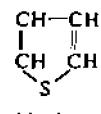
**hetastarch.** A starch derivative containing 90% amylopectin.

**Use:** Blood plasma volume expander.

**heteroaromatic.** See heterocyclic.

**heteroazeotrope.** Azeotropic mixture having more than one liquid phase in equilibrium with the vapor phase at the boiling points.

**heterocyclic.** Designating a closed-ring structure, usually of either 5 or 6 members, in which one or more of the atoms in the ring is an element other than carbon, e.g., sulfur, nitrogen, etc. Examples are pyridine, pyrrole, furan, thiophene, and purine.



thiophene



pyridine

**heterogeneous.** (Latin "different kinds"). Any mixture or solution comprised of two or more substances regardless of whether they are uniformly dispersed. Common examples are such diverse materials as air (a mixture of 20% oxygen and 80% nitrogen), milk, marble, paint, gasoline, blood and mayonnaise. In all such cases, the mixtures can be separated mechanically into their components. "Homogenized" milk is as heterogeneous as regular milk and the term is, strictly speaking, a misnomer.

See homogeneous; mixture.

**heterogeneous catalysis.** See catalysis, heterogeneous.